

*REMARKS/ARGUMENTS**The Present Invention and the Pending Claims*

Claims 1-9 are pending. Claims 1-5 are directed to a method for producing a  $5\alpha$ -pregnane derivative represented by the formula (III). Claims 6-9 are directed to a method for producing (20S)- $7\alpha,21$ -dihydroxy- $20$ -methyl- $5\alpha$ -pregn-3-one represented by the formula (VII).

*Summary of the Claim Amendments*

Claims 1 and 6 have been amended to recite that the compound of formula (I) (claim 1) or (V) (claim 6) is selectively hydrogenated with a transition metal catalyst. This amendment is supported by the specification at, for example, page 14, lines 8-27. No new matter has been added by way of these amendments.

*Summary of the Office Action*

The Office objects to the specification and claims 1-9.

Claims 1, 2, and 5 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Nakazawa et al. (U.S. Patent Application Publication 2003/0181742), as evidenced by Koyakumaru et al. (U.S. Patent Application Publication 2007/0197490).

Claims 1-4 and 6-9 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Nakazawa et al. in combination with Moriarty et al. (*Tetrahedron Letters*, 35(44): 8103-8106 (1994)).

Claims 1-9 have been provisionally rejected for obviousness-type double patenting as allegedly unpatentable over claims 13, 15, 16, and 18 of copending U.S. Patent Application No. 10/594,164 (hereinafter “the ‘164 application”), as evidenced by Koyakumaru et al. (U.S. Patent Application Publication 2007/0197490).

Reconsideration of the pending claims is hereby requested.

*Discussion of the Claim and Specification Objections*

The Office has objected to the specification and claims 1-9. Specifically, in both the specification and claims, the side chain hydroxyl group is referred to as being at the C21-position. The Office contends, however, that based on the IUPAC numbering system, discussed, for example, in Moss, *Pure & Appl. Chem.*, 61(10): 1783-1822 (1989), the hydroxyl is at the C22-position.

According to Moss et al., the parent compound, pregnane, has an ethyl group as a side chain substituted at the C17-position on ring D (see page 1791, section 3S-2.4 and page 1790, Table 1, the first line). In pregnane, only the C20- and C21-carbon atoms are present, and *the C22-carbon atom is absent*. Therefore, since the specification and pending claims are directed to a pregnane derivative, the correct nomenclature is used, in which a methyl group is substituted on the C20-position and a hydroxyl group is substituted on the C21-position.

In view of the foregoing, Applicants submit that no correction of the specification and/or claims is necessary with respect to the nomenclature. Accordingly, Applicants request that the objection to the specification and claims be withdrawn.

*Discussion of the Anticipation Rejection*

Claims 1, 2, and 5 allegedly are anticipated by Nakazawa et al., as evidenced by Koyakumaru et al. Nakazawa et al. discloses a method of preparing  $5\alpha$ -pregnane derivatives as intermediates in the synthesis of a squalamine. The Office concedes that Nakazawa et al. does not explicitly disclose a mixture of formulae (I) and (II). However, it is the Office's position that, as evidenced by Koyakumaru et al., the claimed ene-one compound of formula (II) inherently is formed during the reduction of the compound of formula (I), as disclosed by Nakazawa et al. Formulae II-1 and III-1 of Nakazawa et al. allegedly are the same as a compound of formulae (I) and (III) of pending claims 1, 2, and 5.

Claim 1 has been amended to recite that the compound of formula (II) is selectively hydrogenated with a transition metal catalyst to form a compound of formula (III). Nakazawa et al. does not disclose selectively hydrogenating a compound of formula (II) in the presence of a transition metal catalyst to form a compound of formula (III). Instead, Nakazawa et al. discloses reducing the double bonds of the compound of formula (I) via a

Birch reduction (i.e., alkali metal or alkaline earth metal in the presence of ammonia or amine). See, e.g., paragraphs 0012, 0013, and 0048 of Nakazawa et al. Nakazawa et al. does not disclose or suggest any other methods of reducing the double bonds of the compound of formula (I).

Since Nakazawa et al. does not disclose all of the elements of amended pending claim 1 2, or 5 – inherently or otherwise – Nakazawa et al. does not anticipate the present invention, as defined by those claims. Applicants respectfully request that the anticipation rejection of claims 1, 2, and 5 in view of Nakazawa et al. be withdrawn.

*Discussion of the Obviousness Rejection*

Claims 1-4 and 6-9 allegedly are obvious over Nakazawa et al. in combination with Moriarty et al.

Nakazawa et al. discloses a method of preparing  $5\alpha$ -pregnane derivatives as intermediates in the synthesis of a squalamine.

The Office concedes that Nakazawa et al. does not explicitly disclose a mixture of formulae (I) and (II) as recited in pending claims 1-4. However, it is the Office's position that the claimed ene-one compound of formula (II) inherently is formed during the reduction of the compound of formula (I), as disclosed by Nakazawa et al. Formulae II-1 and III-1 of Nakazawa et al. allegedly are the same as a compound of formulae (I) and (III) of pending claims 1-4.

The Office concedes that Nakazawa et al. does not disclose a compound of formula (V) as recited in pending claims 6-9, in which the C-21 hydroxyl group is protected and the C-7 hydroxyl group optionally is protected. Such compound is not disclosed because Nakazawa et al. does not disclose protecting the hydroxyl group(s) prior to a reduction step, as required by pending claims 6-9.

Moriarty et al. allegedly discloses a hydroxyl protecting group at the C-24 position in a multi-step synthesis of squalamine (see step iv in the production of compound 4, pages 8103-8104). Moriarty et al. also allegedly discloses that the 7-hydroxyl group remains unprotected throughout most of the synthesis. Thus, it is the Office's position that Moriarty

et al. discloses protecting the C-24 hydroxyl group prior to a reduction step, while leaving the C-7 hydroxyl group unprotected.

According to the Office, it would have been obvious to follow the synthesis described by Nakazawa et al., but with the steps reversed (i.e., a protection step followed by reduction), as taught by Moriarty et al. The change of order of process steps based on prior art teachings allegedly is *prima facie* obvious in the absence of new or unexpected results.

Applicants traverse this rejection based on the following discussion.

As discussed above, independent claims 1 and 6 have been amended to recite that the compound of formula (II) (claim 1) or formula (V) (claim 6) is selectively hydrogenated with a transition metal catalyst. Nakazawa et al. does not disclose or suggest selectively hydrogenating double bonds with a transition metal catalyst. Nakazawa et al. only describes reducing the double bonds of the compound of formula (I) via a Birch reduction. Similarly, Moriarty et al. describes reducing compound **5** via a Birch reduction with lithium in the presence of ammonia to form compound **6**. Moriarty et al. does not describe any other type of double bond reduction step.

As a result, Nakazawa et al. and Moriarty et al., separately or in combination, do not disclose all of the elements of any of the amended pending claims. Moreover, the Office provides no credible reason why one of ordinary skill in the art would have modified the synthesis of Nakazawa et al. in the manner necessary to provide the present invention as defined by any of the pending claims, especially selectively hydrogenating a compound of formula (II)/(V) in the presence of a transition metal catalyst to form a compound of formula (III)/(VII).

In view of the foregoing, the combination of Nakazawa et al. and Moriarty et al. does not render the present invention as defined by any of claims 1-4 and 6-9 obvious. As such, the obviousness rejection in view thereof should be withdrawn.

*Discussion of the Obviousness-type Double Patenting Rejection*

Claims 1-9 have been provisionally rejected for obviousness-type double patenting as allegedly unpatentable over certain claims of the '164 application, as evidenced by Koyakumaru et al.

Applicants submit herewith a terminal disclaimer with respect to the '164 application, merely as an administrative convenience to remove the obviousness-type double patenting rejection. See *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20 U.S.P.Q.2d 1392 (Fed. Cir. 1991). The terminal disclaimer is not an admission that the subject matter of the present claims is obvious over the claims of the '164 application.

In view of the foregoing, the obviousness-type double patenting rejection should be withdrawn.

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

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